

CLAIMS

What is claimed is:

- 5 1. An isolated nucleic acid encoding a mammalian resistin, or a
fragment thereof.
2. The isolated nucleic acid of claim 1, wherein said nucleic acid shares
at least about 30% sequence identity with an nucleic acid encoding at least one of
10 mouse *resistin* (SEQ ID NO:1) and human *resistin* (SEQ ID NO:3).
3. The isolated nucleic acid of claim 2, wherein said nucleic acid shares
at least about 30% sequence identity with a nucleic acid having the sequence of SEQ
ID NO:1.
- 15 4. The isolated nucleic acid of claim 2, wherein said nucleic acid shares
at least about 30% sequence identity with a nucleic acid having the sequence of SEQ
ID NO:3.
- 20 5. An isolated nucleic acid encoding a mammalian resistin, wherein the
amino acid sequence of said resistin shares at least about 30% sequence identity with
an amino acid sequence of at least one of (SEQ ID NO:2) and (SEQ ID NO:4).
6. The isolated nucleic acid of claim 5, wherein said amino acid
25 sequence of said resistin shares at least about 30% sequence identity with an amino
acid sequence of (SEQ ID NO:2).
7. The isolated nucleic acid of claim 5, wherein said amino acid
30 acid sequence of (SEQ ID NO:4).

8. An isolated polypeptide comprising a mammalian resistin.

9. The isolated polypeptide of claim 8, wherein said mammalian
5 resistin shares at least about 30% sequence identity with an amino acid sequence of at least one of SEQ ID NO:2 and SEQ ID NO:4.

10. The isolated polypeptide of claim 9, wherein said mammalian
10 resistin shares at least about 30% sequence identity with an amino acid sequence of SEQ ID NO:2.

11. The isolated polypeptide of claim 9, wherein said mammalian
15 resistin shares at least about 30% sequence identity with an amino acid sequence of SEQ ID NO:4.

12. The nucleic acid of claim 1, said nucleic acid further comprising a
nucleic acid encoding a tag polypeptide covalently linked thereto.

13. The nucleic acid of claim 12, wherein said tag polypeptide is
20 selected from the group consisting of a myc tag polypeptide, a glutathione-S-transferase tag polypeptide, a green fluorescent protein tag polypeptide, a myc-pyruvate kinase tag polypeptide, a His6 tag polypeptide, an influenza virus hemagglutinin tag polypeptide, a flag tag polypeptide, and a maltose binding protein tag polypeptide.

14. The nucleic acid of claim 1, said nucleic acid further comprising a
nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

15. A vector comprising the nucleic acid of claim 1.

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16. The vector of claim 15, said vector further comprising a nucleic acid encoding a promoter/regulatory sequence operably linked thereto.

17. A recombinant cell comprising the isolated nucleic acid of claim 1.

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18. A recombinant cell comprising the vector of claim 15.

19. An isolated nucleic acid complementary to the nucleic acid of claim 1, said complementary nucleic acid being in an antisense orientation.

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20. The isolated nucleic acid of claim 19, wherein said nucleic acid shares at least about 30% identity with a nucleic acid complementary with a nucleic acid having the sequence of at least one of mouse *resistin* (SEQ ID NO:1) and human *resistin* (SEQ ID NO:3).

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21. A recombinant cell comprising the isolated nucleic acid of claim 19.

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22. An antibody that specifically binds with a mammalian resistin polypeptide, or a fragment thereof.

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23. The antibody of claim 22, wherein said antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, and a synthetic antibody.

24. An antidiabetic composition comprising the antibody of claim 22 and a pharmaceutically-acceptable carrier.

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25. An antidiabetic composition comprising the isolated nucleic acid of claim 19 and a pharmaceutically-acceptable carrier

25. A composition comprising the isolated nucleic acid of claim 1 and a pharmaceutically-acceptable carrier.
- 5 27. A knock-out targeting vector, said vector comprising a first nucleic acid portion encoding a nucleic acid comprising a sequence 5' of the open reading frame encoding *resistin* and a second nucleic acid portion comprising a nucleic acid sequence 3' of the open reading frame encoding a mammalian *resistin*.
- 10 28. The knock-out targeting vector of claim 27, said vector further comprising a nucleic acid encoding a selectable marker covalently linked thereto.
- 15 29. The knock-out vector of claim 28, wherein said first and second nucleic acid portions flank said nucleic acid encoding said selectable marker.
30. A recombinant cell comprising the knock-out targeting vector of claim 27.
- 20 31. A transgenic non-human mammal comprising the knock-out targeting vector of claim 27.
32. The transgenic mammal of claim 31, wherein the mammal is a rodent.
- 25 33. A transgenic non-human mammal comprising the isolated nucleic acid of claim 1.
- 30 34. A method of alleviating type 2 diabetes, said method comprising administering to a patient afflicted with type 2 diabetes a glucose uptake-enhancing amount of the composition of claim 24.

- 34 35. A method of alleviating type 2 diabetes, said method comprising administering to a patient afflicted with type 2 diabetes a glucose uptake-enhancing amount of the composition of claim 25.
- 5 35 36. A method of alleviating Syndrome X, said method comprising administering to a patient afflicted with Syndrome X a glucose uptake-enhancing amount of the composition of claim 24.
- 10 36 37. A method of alleviating Syndrome X, said method comprising administering to a patient afflicted with Syndrome X a glucose uptake-enhancing amount of the composition of claim 25.
- 15 37 38. A method of treating type 2 diabetes, said method comprising administering to a patient afflicted with type 2 diabetes a glucose uptake-enhancing amount of a composition selected from the group consisting of the composition of claim 24 and the composition of claim 25.
- 20 38 39. A method of treating Syndrome X, said method comprising administering to a patient afflicted with Syndrome X a glucose uptake-enhancing amount of a composition selected from the group consisting of the composition of claim 24 and the composition of claim 25.
- 25 39 40. A method of alleviating type 2 diabetes, said method comprising administering to a patient afflicted with type 2 diabetes a resistin-inhibiting amount of a composition selected from the group consisting of the composition of claim 24 and the composition of claim 25.
- 30 40 41. A method of alleviating Syndrome X, said method comprising administering to a patient afflicted with Syndrome X a resistin-inhibiting amount of a

composition selected from the group consisting of the composition of claim 24 and the composition of claim 25.

41 42. A method of treating type 2 diabetes, said method comprising
5 administering to a patient afflicted with type 2 diabetes a resistin-inhibiting amount of
a composition selected from the group consisting of the composition of claim 24 and
the composition of claim 25.

42 43. A method of treating Syndrome X, said method comprising
10 administering to a patient afflicted with Syndrome X a resistin-inhibiting amount of a
composition selected from the group consisting of the composition of claim 24 and the
composition of claim 25.

43 44. A method of identifying a compound that affects expression of
15 resistin in a cell, said method comprising contacting a cell with a test compound and
comparing the level of resistin expression in said cell with the level of resistin
expression in an otherwise identical cell not contacted with said test compound,
wherein a higher or lower level of resistin expression in said cell contacted with said
test compound compared with the level of resistin expression in said otherwise
20 identical cell not contacted with said test compound is an indication that said test
compound affects expression of resistin in a cell.

44 45. A compound identified by the method of claim 44.

25 45 46. A method of identifying a compound that reduces expression of
resistin in a cell, said method comprising contacting a cell with a test compound and
comparing the level of resistin expression in said cell with the level of resistin
expression in an otherwise identical cell not contacted with said test compound,
wherein a lower level of resistin expression in said cell contacted with said test
30 compound compared with the level of resistin expression in said otherwise identical

cell not contacted with said test compound is an indication that said test compound reduces expression of resistin in a cell.

46 47. A compound identified by the method of claim 46.

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47 48. A method of determining whether a test compound is a candidate antidiabetic drug candidate, said method comprising contacting a cell comprising a nucleic encoding resistin with a test compound, and comparing the level of expression of resistin in said cell with the level of expression of resistin in an otherwise identical
10 cell which is not contacted with said test compound, whereby a lower level of expression of resistin in said cell contacted with said test compound compared with the level of expression of resistin in said otherwise identical cell not contacted with said test compound is an indication that said test compound is a candidate antidiabetic drug candidate.

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48 49. A method of determining whether a test compound is a candidate drug for treatment of Syndrome X, said method comprising contacting a cell comprising a nucleic encoding resistin with a test compound, and comparing the level of expression of resistin in said cell with the level of expression of resistin in an
20 otherwise identical cell which is not contacted with said test compound, whereby a lower level of expression of resistin in said cell contacted with said test compound compared with the level of expression of resistin in said otherwise identical cell not contacted with said test compound is an indication that said test compound is a candidate drug for treatment of Syndrome X.

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49 50. A method of determining whether a test compound is a candidate antidiabetic drug candidate, said method comprising contacting a cell comprising a PPAR γ receptor and a nucleic encoding resistin with a test compound, and comparing the level of expression of resistin in said cell with the level of expression of resistin in
30 an otherwise identical cell which is not contacted with said test compound, whereby a

lower level of expression of resistin in said cell contacted with said test compound compared with the level of expression of resistin in said otherwise identical cell not contacted with said test compound is an indication that said test compound is a candidate antidiabetic drug candidate.

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50 51. A method of increasing glucose uptake by a cell, said method comprising contacting a cell expressing resistin with a resistin-reducing amount of an anti-resistin compound, thereby increasing glucose uptake by said cell.

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51 52. The method of claim 51, wherein said cell expressing resistin is selected from the group consisting of an adipocyte, a recombinant cell transfected with an isolated nucleic acid encoding *resistin*, a muscle cell line, a liver cell line, a primary culture cell from skeletal muscle, a primary culture adipocyte cell, and a primary culture hepatocyte.

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52 53. A method of increasing insulin-stimulated glucose uptake by a cell, said method comprising contacting a cell expressing resistin with insulin and further contacting said cell with a resistin-reducing amount of an anti-resistin compound, thereby increasing insulin-stimulated glucose uptake by said cell.

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53 54. A method of diagnosing type 2 diabetes in a previously undiagnosed mammal, said method comprising obtaining a biological sample from said mammal, assessing the level of resistin in said biological sample, and comparing the level of resistin in said biological sample with the level of resistin in a biological sample obtained from a like mammal not afflicted with type 2 diabetes, wherein a higher level of resistin in said biological sample from said mammal compared with the level of resistin in said biological sample from said like mammal is an indication that said mammal is afflicted with type 2 diabetes, thereby diagnosing type 2 diabetes in said previously undiagnosed mammal.

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54 55. The method of claim 54, wherein said biological sample is selected from the group consisting of a blood sample, a white adipose tissue sample, and a brown adipose tissue sample.

5 55 56. A method of diagnosing Syndrome X in a previously undiagnosed mammal, said method comprising obtaining a sample from said mammal, assessing the level of resistin in said sample, and comparing the level of resistin in said sample with the level of resistin in a sample obtained from a like mammal not afflicted with Syndrome X, wherein a higher level of resistin in said sample from said mammal
10 compared with the level of resistin in said sample from said like mammal is an indication that said mammal is afflicted with Syndrome X, thereby diagnosing Syndrome X in said previously undiagnosed mammal.

56 57. A method of assessing the effectiveness of a treatment for type 2
15 diabetes in a mammal, said method comprising assessing the level of resistin in a sample obtained from a mammal prior to treatment of said mammal for type 2 diabetes, and comparing the level of resistin in said sample with the level of resistin in a sample obtained from said mammal during the course of or following treatment for type 2 diabetes, wherein a lower level of resistin in said sample obtained prior to treatment
20 compared with said level of resistin in said sample obtained during the course of or following treatment for type 2 diabetes is an indication of the effectiveness of said treatment for type 2 diabetes in said mammal.

57 58. A method of assessing the effectiveness of a treatment for
25 Syndrome X in a mammal, said method comprising assessing the level of resistin in a sample obtained from a mammal prior to treatment of said mammal for Syndrome X, and comparing the level of resistin in said sample with the level of resistin in a sample obtained from said mammal during the course of or following treatment for Syndrome X, wherein a lower level of resistin in said sample obtained prior to treatment
30 compared with said level of resistin in said sample obtained during the course of or

following treatment for Syndrome X is an indication of the effectiveness of said treatment for Syndrome X in said mammal.

58 59. A method of assessing the response in a mammal to TZD, said
5 method comprising assessing the level of resistin in a sample obtained from a mammal
prior to administration of TZD to said mammal, administering TZD to said mammal,
and assessing the level of resistin in a sample obtained from said mammal during or
after administration of TZD, wherein a higher or lower level of resistin in said sample
10 obtained during or after administration of TZD to said mammal compared with said
level of resistin in said sample obtained during or after administration of TZD is an
indication of the response to TZD in said mammal, thereby assessing the response to
TZD in said mammal.

59 60. A method of assessing the response in a mammal to a compound
15 that affects PPAR γ -mediated signaling, said method comprising assessing the level of
resistin in a sample obtained from a mammal prior to administration of said compound
to said mammal, administering said compound to said mammal, assessing the level of
resistin in a sample obtained from said mammal during or after administration of said
compound, and comparing said level of resistin in said sample obtained during or after
20 administration of said compound to said mammal with said level of resistin in said
sample obtained prior to administration of said compound to said mammal, wherein a
higher or lower level of resistin in said sample obtained during or after administration
of said compound to said mammal compared with said level of resistin in said sample
obtained prior to administration of said compound to said mammal is an indication of
25 the response in said mammal to said compound, thereby assessing the response in said
mammal to a compound that affects PPAR γ -mediated signaling.

60 61. A method of detecting a mutation in a *resistin* allele in a human,
said method comprising comparing the nucleic acid sequence encoding *resistin* of a
30 human suspected of having a mutation in a *resistin* allele with the nucleic acid

sequence encoding *resistin* obtained from a normal human not having a mutation in a *resistin* allele, wherein any difference between said nucleic acid sequence of said human suspected of having a mutation in said *resistin* allele and said nucleic acid sequence encoding *resistin* of said normal human not having a mutation in said *resistin* allele detects a mutation in said *resistin* allele in said human.

61 62. A method of detecting a mutation in a *resistin* allele in a human, said method comprising comparing the genomic nucleic acid sequence encoding *resistin* of a human suspected of having a mutation in a *resistin* allele with the genomic nucleic acid sequence encoding *resistin* obtained from a normal human not having a mutation in a *resistin* allele, wherein any difference between said genomic nucleic acid sequence of said human suspected of having a mutation in said *resistin* allele and said genomic nucleic acid sequence encoding *resistin* of said normal human not having a mutation in said *resistin* allele detects a mutation in said *resistin* allele in said human.

62 63. A method of treating a human patient afflicted with type 2 diabetes, said method comprising obtaining a biological sample from a human donor, isolating any cells from said biological sample, transfecting said cells with the isolated nucleic acid of claim 19, wherein when said nucleic acid is expressed in said cells expression of resistin in said cells is inhibited, and administering said cells to said human patient, wherein the presence of said cells in said human patient effects treatment of said type 2 diabetes.

63 64. The method of claim 63, wherein said human donor is not suffering from type 2 diabetes and wherein said human donor is syngeneic with said human patient.

64 65. The method of claim 63, wherein said human donor is said human patient.

65 ~~66~~. The method of claim 63, wherein said isolated nucleic acid is operably linked to a promoter/regulatory sequence.

66 ~~67~~. A method of treating a human patient afflicted with type 2 diabetes,
 5 said method comprising obtaining a biological sample from a human donor, isolating any cells from said biological sample, transfecting said cells with the knock-out targeting vector of claim 27, wherein when said cells are transfected with said knock-out targeting vector expression of resistin in said cells is inhibited, and administering said cells to said human patient, wherein the presence of said cells in said human
 10 patient effects treatment of said type 2 diabetes.

67 ~~68~~. A method of increasing blood glucose levels in a mammal, said method comprising administering a effective amount of an isolated resistin polypeptide to said mammal, thereby increasing blood glucose levels in said mammal.

15 68 ~~69~~. A method of increasing blood sugar level in a mammal, said method comprising administering to said mammal an effective amount of resistin, thereby increasing blood sugar level in said mammal.

20 69 ~~70~~. A method of increasing blood sugar level in a mammal, said method comprising administering to said mammal an isolated recombinant cell transfected with an isolated nucleic acid encoding resistin wherein said nucleic acid is expressed in said cell, wherein the presence of said recombinant cells in said mammal effects an increased blood sugar level in said mammal.

25 70 ~~71~~. A method of treating a human patient afflicted with type 2 diabetes, said method comprising administering to said human patient the recombinant cell of claim 21, wherein the presence of said recombinant cell in said human patient effects treatment of said type 2 diabetes.

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- 11 72. A method of treating a human patient afflicted with type 2 diabetes,
said method comprising administering to said human patient the recombinant cell of
claim 30, wherein the presence of said recombinant cell in said human patient effects
treatment of said type 2 diabetes.
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- 12 73. A method of increasing blood sugar level in a mammal, said
method comprising administering to said mammal the recombinant cell of claim 17,
wherein the presence of said recombinant cell in said mammal effects an increased
blood sugar level in said mammal
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- 13 74. A kit for alleviating type 2 diabetes, said kit comprising a resistin-
inhibiting amount of the composition of claim 24, said kit further comprising an
applicator, and an instructional material for the use thereof.
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- 14 75. A kit for alleviating type 2 diabetes, said kit comprising a resistin-
inhibiting amount of the composition of claim 25, said kit further comprising an
applicator, and an instructional material for the use thereof.
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- 15 76. A kit for treating type 2 diabetes, said kit comprising a resistin-
inhibiting amount of the composition of claim 24, said kit further comprising an
applicator, and an instructional material for the use thereof.
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- 16 77. A kit for treating type 2 diabetes, said kit comprising a resistin-
inhibiting amount of the composition of claim 25, said kit further comprising an
applicator, and an instructional material for the use thereof.
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- 17 78. A kit for alleviating Syndrome X, said kit comprising a resistin-
inhibiting amount of the composition of claim 24, said kit further comprising an
applicator, and an instructional material for the use thereof.

78 79. A kit for alleviating Syndrome X, said kit comprising a resistin-inhibiting amount of the composition of claim 25, said kit further comprising an applicator, and an instructional material for the use thereof.

5 79 80. A kit for treating Syndrome X, said kit comprising a resistin-inhibiting amount of the composition of claim 24, said kit further comprising an applicator, and an instructional material for the use thereof.

80 81. A kit for treating Syndrome X, said kit comprising a resistin-inhibiting amount of the composition of claim 25, said kit further comprising an applicator, and an instructional material for the use thereof.

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